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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,047	12/07/2000	Edwin F. Ullman	BEH-7385	9672

34500 7590 11/13/2007

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EXAMINER	
VENCI, DAVID J	
ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
11/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/732,047	ULLMAN ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 28, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of Notice of Appeal and Appeal Brief, filed May 3, 2007, and June 28, 2007, respectively. Examiner has carefully considered Applicants' Appeal Brief and arguments contained therein, and it has been principally determined that Applicants' Appeal Brief and arguments contained therein technically obviate outstanding rejection to claims 44-46 under 35 U.S.C. § 103(a) in view of Bronstein *et al.* (US 6,243,980) and Pease *et al.* (US 5,709,994), as set forth in the Office Action dated February 6, 2007.

With modification, Examiner herein maintains original grounds for rejection of claims 44-46, under 35 U.S.C. § 103(a) in view of Bronstein *et al.* (US 6,243,980) and Pease *et al.* (US 5,709,994), and raises new issues for Applicants' consideration in view of the teachings of Smith *et al.*, 82 J. PHYS. CHEM. 2291 (1978), and Holtz *et al.*, 274 J. BIOL. CHEM. 8351 (1999). The teachings of Smith *et al.* and Holtz *et al.* raise new issues of inherency pertaining to the claimed "sensitizer causing formation of reactive oxygen, which cleaves the cleavable linker", which Examiner asserts, is taught by Bronstein *et al.*

The finality of the Office Action dated February 6, 2007, is withdrawn.

Claims 44-46 are pending.

Specification

Amendment to the paragraph on page 9, lines 5-22 (as last amended November 20, 2006) is objected to because of the following informalities:

> The sentence "When peroxide or singlet oxygen is generated, an oxidant cleavable linker is cleaved, releasing multiple products" (emphasis added) is not clear. How cleaving *a single* linker results in release of "multiple products" is not clear.

Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bronstein *et al.* (US 6,243,980) in view of Pease *et al.* (US 5,709,994).

Bronstein *et al.* describe a method for determining the presence or concentration of an analyte in a medium, said method comprising:

(1) providing a reacting mixture comprising in combination:

(a) a medium[1] suspected of containing an analyte;[2]

(b) a first specific binding pair member[3] bound to a solid support;[4]

(c) a second specific binding pair member[5] bound to a sensitizer[6,7] capable in its excited state of generating a reactive oxygen species[8], wherein the proximity of the first specific

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[1] See Abstract, first sentence, "sample".
[2] See Title, "protease inhibitor".
[3] See Fig. 3, $OPO_3^=$.
[4] See Fig. 3, adamantyl moiety.
[5] See col. 5, lines 65-66, "second binding ligand pair".
[6] See col. 5, lines 66-67, "conjugated with an enzyme[...] such as alkaline phosphatase" (paraphrasing mine).
[7] See *also*, Holtz *et al.*, 274 J. BIOL. CHEM. 8351 (1999), *noting* their description of an "active site" sensitizer or a "Ser-102" sensitizer on alkaline phosphatase, either of which are capable of generating reactive oxygen (see Scheme 1, "RO^{-}").
[8] See Fig. 3, oxyanion; col. 6, lines 23-25, "alkaline phosphatase, forms a negatively charged substituent (e.g., an oxyanion)".

binding pair member with the second specific binding pair member is modulated by the presence of the analyte;[9]

(d) digoxigenin-linked biotin[10] linked to the support[11] through a reactive oxygen cleavable linker;[12]

(2) incubating the reaction mixture;[13]

(3) exciting the sensitizer, said excitation of the sensitizer causing the formation of reactive oxygen[14], which cleaves the cleavable linker[15,16] and releases digoxigenin-linked biotin from the support;[17] and

(4) detecting the released digoxigenin-linked biotin, the amount thereof being related to the amount of analyte in said medium.[18]

Bronstein *et al.* do not describe "water-insoluble" solid supports.

However, Pease *et al.* describe "water-insoluble" solid supports (see Title, "matrices") for general use in chemiluminescence assays (see Abstract, fifth sentence).

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[9] See Abstract, fifth and sixth sentences, "Substrate cleavage, if not inhibited, is allowed to occur, and any unbound cleaved fragments are removed. An enzyme complexed with the second member of the second ligand binding pair is added, and allowed to bind to any of the (uncleaved) first member of the second ligand binding pair remaining".
[10] See col. 7, lines 10-12, "labels for either end of the peptide are: Biotin... and Digoxin (digoxigenin labeled peptide)" (paraphrasing mine).
[11] See Fig. 3, adamantyl moiety.
[12] See Abstract, first sentence, "1,2-dioxetanes"; see *also*, Fig. 3, 1,2-dioxetane moiety.
[13] See Abstract, fifth sentence, "Substrate cleavage, if not inhibited, is allowed to occur".
[14] See col. 6, lines 23-25, "alkaline phosphatase, forms a negatively charged substituent (e.g., an oxyanion)")
[15] See col. 6, lines 25-27, "This [oxyanion] destabilizes the dioxetane, thereby causing the dioxetane to decompose to form two carbonyl-containing groups") (paraphrasing mine).
[16] See *also*, Smith *et al.*, 82 J. PHYS. CHEM. 2291 (1978), *noting* their description of oxygen-containing "excited dioxetane" or "biradical", either of which perform bond cleavage (see Fig. 4).
[17] See Fig. 3, *noting* the release of the adamantyl moiety from the oxyanion/$OPO_3^=$ group.

It would have been obvious for a person of ordinary skill to perform the analyte determination of Bronstein *et al.* with "water-insoluble" solid supports because Pease *et al.* discovered "water-insoluble" solid supports with "delayed luminescence" lifetimes, which can be modulated as a function of structure and/or composition (see col. 8, lines 1-9).

[18] See Abstract, last sentence, "when the dioxetane is caused to decompose, energy is transferred to the fluorescing entity, which releases light of a wavelength recognizably distinct".

Response to Arguments

Specification

In prior Office Action, Examiner objected to the amendment to the paragraph on page 5, lines 1-14 was because the mechanism by which "release of the substrate with formation of a first binding site may be accompanied by unmasking of at least some of a second binding site" was considered mechanistically unclear.

In response, Applicants provide reference to, and indicate original support for, the aforementioned concept in the specification at p. 5, lines 24-26 for distinct amino (*e.g.*, a ureido nitrogen) functional group, and a biotin functional group. Accordingly, this objection is withdrawn.

In prior Office Action, Examiner objected to the amendment to the paragraph on page 9, lines 5-22 (as last amended November 20, 2006) because the sentence "When peroxide or singlet oxygen is generated, an oxidant cleavable linker is cleaved, releasing multiple products" (emphasis added) is not clear. How cleaving *a single* linker results in release of "multiple products" is not clear.

In response, Applicants point out, and Examiner acknowledges, that the specification paragraph on page 9, lines 5-22 describes "multiple copies of a substrate" attached to a support or surface. However, the paragraph does not explain how cleaving *a single* linker results in release of "multiple products". In other words, it is not clear how cleaving one linker results in release of more than one product.

Claim Rejections - 35 USC § 112

In prior Office Action, claims 44-46 were rejected under 35 U.S.C. 112, second paragraph, because the term "water-insoluble" was considered indefinite. This rejection has been principally withdrawn.

Claim Rejections - 35 USC § 103

In prior Office Action, claims 44-46 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bronstein *et al.* (US 6,243,980) in view of Pease *et al.* (US 5,709,994).

Applicants' Appeal Brief and arguments contained therein contain good technical reasons for distinguishing Applicants' invention over the cited portions of the prior art. Examiner believes the revised rejection of claims 44-46 under 35 U.S.C. 103(a), set forth *supra*, addresses and obviates Applicants' arguments.

Specifically, the revised rejection of claims 44-46 under 35 U.S.C. 103(a), set forth *supra*, no longer references Bronstein's discussion of photooxygenation (i.e., col. 5, lines 36-37) or Bronstein's homogeneous assay embodiment (*i.e.*, Fig. 14).

In addition, Examiner introduces the teachings of Smith *et al.*, 82 J. PHYS. CHEM. 2291 (1978), and Holtz *et al.*, 274 J. BIOL. CHEM. 8351 (1999), who provide unequivocal proof of the inherency of reactive oxygen, which cleaves Bronstein's 1,2-dioxetane linker.

Reconsideration is respectfully requested.

Conclusion

No claims are allowable at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Assistant Examiner
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djv

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